

~~monomer. Hereon in this disclosure, "CKPV dimer" will be the term used to identify this form of a KPV dimer, i.e., two CKPV monomers linked through a disulfide bond, i.e., VPKC (SEQ ID NO: 8) -s-s-CKPV (SEQ ID NO: 8). It is contemplated that other KPV dimers may be used in the disclosed composition.~~

The present invention is directed to a system for treating uro-genital conditions. One aspect of this invention involves a treatment comprising one or more polypeptides with an amino acid sequence including KPV (SEQ ID NO: 1), MEHFRWG (SEQ ID NO: 2), HFRWGKPV (SEQ ID NO: 3), VPKC (SEQ ID NO: 5) -s-s-CKPV (SEQ ID NO: 5) or SYSMEHFRWGKPV (SEQ ID NO: 4) for treatment of uro-genital conditions. VPKC-s-s-CKPV is an example of a "KPV dimer" wherein a disulfide bond exists between N-terminal cysteines of each monomer. Hereon in this disclosure, "CKPV dimer" will be the term used to identify this form of a KPV dimer, i.e., two CKPV monomers linked through a disulfide bond, i.e., VPKC (SEQ ID NO: 5) -s-s-CKPV (SEQ ID NO: 5). It is contemplated that other KPV dimers may be used in the disclosed composition.

### **In the Detailed Description of the Preferred Embodiments**

Please replace Paragraph 43 as follows:

~~In another aspect of the invention, a pharmaceutical composition for use in the treatment of urogenital conditions comprises a KPV dimer, preservative agents, a solvent, an alkalizer, Carbopol®, and a gelatinizing agent. The composition may further comprise a chelating agent. These ingredients may be modified, replaced or eliminated. A KPV dimer is preferred over other useful~~

~~alpha-MSH peptides as it has been shown to be more efficacious in treating vaginitis. See, Example XII below.~~

In another aspect of the invention, a pharmaceutical composition for use in the treatment of urogenital conditions comprises a CKPV dimer (SEQ ID NO: 5), preservative agents, a solvent, an alkalizer, Carbopol®, and a gelatinizing agent. The composition may further comprise a chelating agent. These ingredients may be modified, replaced or eliminated. A CKPV dimer (SEQ ID NO: 5) is preferred over other useful alpha-MSH peptides as it has been shown to be more efficacious in treating vaginitis. See, Example XII below.

Please replace Paragraph 44 as follows:

~~In another aspect of the invention, a pharmaceutical composition is disclosed for use in the treatment of uro-genital conditions wherein said composition comprises an acrylic acid-based polymer, for example, Carbopol®, NF; propylparaben, NF; methylparaben, NF; propylene glycol, USP; EDTA, USP; the CKPV dimer, API; 2 M NaOH; and sterile water for injection, USP. Disclosed below is at least one embodiment of the invention presented in a 0.1% CKPV dimer batch of the composition weighing approximately 4Kg. A contemplate range of percentages of individual components of the invention are disclosed for different size quantities of the invention.~~

In another aspect of the invention, a pharmaceutical composition is disclosed for use in the treatment of uro-genital conditions wherein said composition comprises an acrylic acid-based polymer, for example, Carbopol®,

NF; propylparaben, NF; methylparaben, NF; propylene glycol, USP; EDTA, USP; CKPV (SEQ ID NO: 5), API; 2 M NaOH; and sterile water for injection, USP.

Disclosed below is at least one embodiment of the invention presented in a 0.1% CKPV dimer (SEQ ID NO: 5) batch of the composition weighing approximately 4Kg. A contemplate range of percentages of individual components of the invention are disclosed for different size quantities of the invention.

Please replace Paragraph 53 as follows:

~~The CKPV dimer is one form of KPV dimer that may be used with the present invention. The amount of the CKPV dimer for use in the disclosed composition ranges from at least about 2-6g or 0.05-0.15% of the composition. A preferred amount of the CKPV dimer is at least about 4g or 0.1% of the composition.~~

The CKPV (SEQ ID NO: 5) dimer is one form of dimer that may be used with the present invention. The amount of CKPV (SEQ ID NO: 5) for use in the disclosed composition ranges from at least about 2-6g or 0.05-0.15% of the composition. A preferred amount of CKPV dimer (SEQ ID NO: 5) is at least about 4g or 0.1% of the composition.

Please amend Paragraph 58 as follows:

A 4 Kg. 0.1 percent CKPV (SEQ ID NO: 5) dimer gel batch of the composition preferably comprises:

Carbopol®, NF	80.0g
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Propylparaben, NF	2.0g
Methylparaben, NF	6.0g
Propylene glycol, USP	400.0g
EDTA, USP	4.0g
The CKPV <u>(SEQ ID NO:5)</u> dimer, API	4.0g
2M NaOH Solution	Quantity sufficient to pH 4.0 $\pm$ 0.1
Sterile water for injection, USP	3504g

Please amend Paragraph 59 as follows:

As disclosed above and below, an effective amount of the CKPV (SEQ ID NO: 5) dimer, when used as a therapeutic, ranges in picomolar to nanomolar concentrations. Micromolar concentrations are more potently effective. The dosage of the pharmaceutical composition disclosed herein ranges from 50-150  $\mu\text{g/ml}$ . A preferred dose of the pharmaceutical composition described herein is 100  $\mu\text{g/ml}$ .

Please replace Paragraph 61 as follows:

~~The peptides used in the following examples include: the CKPV dimer, alpha-MSH (1-13) (SEQ ID NO: 4), (4-10) (SEQ ID No: 2), (6-13) (SEQ ID NO: 3), and (11-13) (SEQ ID NO: 1), all of which were N-acetylated and C-amidated, and ACTH (1-39) and (18-39) (CLIP). These peptides were prepared by solid-phase peptide synthesis and purified by reversed phased high performance liquid chromatography. Figure 16 shows a representation of one chemical structure for a KPV dimer, i.e., the CKPV dimer. Dimers can be formed by adding cysteines at the N-termini of any of the above polypeptides and allowing the cysteines of two polypeptides to form a disulfide bond. Both homo-dimers and hetero-dimers can be formed using this method.~~

The peptides used in the following examples include: a dimer of CKPV (SEQ ID NO: 5), alpha-MSH (1-13) (SEQ ID NO: 4), (4-10) (SEQ ID No: 2), (6-13) (SEQ ID NO: 3), and (11-13) (SEQ ID NO: 1), all of which were N-acetylated and C-amidated, and ACTH (1-39) (SEQ ID NO: 9) and (18-39) (SEQ ID NO: 10) (CLIP). These peptides were prepared by solid-phase peptide synthesis and purified by reversed phased high performance liquid chromatography. Figure 16 shows a representation of one chemical structure for a KPV dimer, i.e., the CKPV dimer (SEQ ID NO: 5). Dimers can be formed by adding cysteines at the N-termini of any of the above polypeptides and allowing the cysteines of two polypeptides to form a disulfide bond. Both homo-dimers and hetero-dimers can be formed using this method.

Please replace Paragraph 62 as follows:

~~A KPV dimer may be formed when the N-termini of two KPV peptides are joined by a linker. VPKC (SEQ ID NO: 8) -s-s CKPV (SEQ ID NO: 8) is an example of a KPV dimer formed by adding a cysteine at the N-terminal of a KPV peptide and allowing the cysteines of, then, two CKPV peptides to form a disulfide bond (-s-s). In other words, VPKC (SEQ ID NO: 8) -s-s CKPV (SEQ ID NO: 8) is formed when two KPV (SEQ ID NO: 1) peptides are linked by a Cys-s-s-Cys linker. The linker can be any kind of chemical bond that links the N-terminals of two KPV peptides together. It is preferred that the linker be Cys-s-s-Cys-, -DCys-s-s-Cys-, -Pen-s-s-Cys-, -Pen-s-s-DCys-, -DPen-s-s-Cys-, -DPen-s-s-DCys-, -DPen-s-s-DPen-, -Pen-s-s-Pen-, hCys-s-s-Cys-, hCys-s-s-DCys-, hCys-s-s-hCys-, -DhCys-s-s-DhCys-, -DhCys-s-s-hCys-, hCys-s-s-Pen-, hCys-s-s-DPen-, or -DhCys-s-s-DPen-~~

A KPV dimer may be formed when the N-termini of two KPV peptides are joined by a linker. VPKC (SEQ ID NO: 5) -s-s CKPV (SEQ ID NO: 5) is an example of a KPV dimer formed by adding a cysteine at the N-terminal of a KPV peptide and allowing the cysteines of, then, two CKPV peptides to form a disulfide bond (-s-s-). In other words, VPKC (SEQ ID NO: 5) -s-s CKPV (SEQ ID NO: 5) is formed when two KPV (SEQ ID NO: 1) peptides are linked by a -Cys-s-s-Cys- linker. The linker can be any kind of chemical bond that links the N-terminals of two KPV peptides together. It is preferred that the linker be -Cys-s-s-Cys-, -DCys-s-s-Cys-, -Pen-s-s-Cys-, -Pen-s-s-DCys-, -DPen-s-s-Cys-, -DPen-s-

s-DCys-, -DPen-s-s-DPen-, -Pen-s-s-Pen-, -hCys-s-s-Cys-, -hCys-s-s-DCys-, -hCys-s-s-hCys-, -DhCys-s-s-DhCys-, -DhCys- s-s-hCys-, -hCys-s-s-Pen-, -hCys-s-s-DPen-, or -DhCys-s-s-DPen-.

Please replace Paragraph 62 as follows:

It is more preferred that the linker be -Cys-Cys-. The term "Pen" refers to Penicillamine. The Term "Cys" refers to Cysteine. The Term "hCys" refers to homocysteine. The prefix "D" refers to the *dextro*-form of an amino acid.

Accordingly, it is preferred that the KPV dimer be VPK-Cys (SEQ ID NO: 5) -s-s-Cys-KPV (SEQ ID NO: 5), VPK-DCys (SEQ ID NO: 6)-s-s-Cys-KPV (SEQ ID NO: 5), VPK-Pen- s-s-Cys-KPV (SEQ ID NO: 5), VPK-Pen- s-s-DCys-KPV (SEQ ID NO: 6), VPK-DPen-s-s-Cys-KPV (SEQ ID NO: 5), VPK-DPen-s-s-DCys-KPV (SEQ ID NO: 6), VPK-DPen-s-s-DPen-KPV, VPK-Pen-s-s-Pen-KPV, VPK-hCys (SEQ ID NO: 7)-s-s-Cys-KPV (SEQ ID NO: 5), VPK-hCys (SEQ ID NO: 7)-s-s-DCys-KPV (SEQ ID NO: 6), VPK-hCys (SEQ ID NO: 7) -s-s-hCys-KPV (SEQ ID NO: 7) , VPK-DhCys (SEQ ID NO: 8)-s-s-DhCys-KPV (SEQ ID NO: 8), VPK-DhCys (SEQ ID NO: 8)-s-s-hCys-KPV (SEQ ID NO: 7), VPK-hCys (SEQ ID NO: 7) -s-s-Pen-KPV, VPK-hCys (SEQ ID NO: 7)-s-s-DPen-KPV, or VPK-DhCys (SEQ ID NO: 8)-s-s-DPen-KPV. It is more preferred that the KPV dimer a CKPV (SEQ ID NO: 5) dimer, i.e., VPK-Cys (SEQ ID NO: 5) -s-s-Cys-KPV (SEQ ID NO: 5).

Please amend Paragraph 68 as follows:

Cultures of *S. aureus* (ATCC 29213) were obtained from the collection of the Department of Microbiology, Ospedale Maggiore di Milano. *S. aureus* ( $1 \times 10^6$ /ml in Hank's balanced salt solution) was incubated in the presence or absence of alpha-MSH (1-13) (SEQ ID NO: 4), alpha-MSH (11-13) (SEQ ID NO: 1), or the CKPV (SEQ ID NO: 5) dimer at concentrations in the range of  $10^{-15}$  to  $10^{-4}$  M for two hours at 37°C. Cells were then washed in cold distilled water and diluted with HBSS to a concentration of 100 organisms/ml. One-milliliter aliquots were dispensed on blood agar plates and incubated for 24 hours at 37°C. Viability of the microorganisms was estimated from the colonies formed. In another set of experiments, 500 units of urokinase, a *S. aureus* growth enhancer, were also incubated with the bacteria ( $10^5$ /100ml) for four hours at 37°C in a shaking water bath together with the peptides.

Please amend Paragraph 69 as follows:

Figure 1 shows that alpha-MSH (1-13) (SEQ ID NO: 4), alpha-MSH (11-13) (SEQ ID NO: 1), and the CKPV (SEQ ID NO: 5) dimer all inhibited *S. aureus* colony formation. These inhibitory effects occurred over a wide range of concentrations and were significant ( $p > 0.01$ ) with peptide concentrations of  $10^{-12}$  to  $10^{-4}$  M. Figure 2 shows that alpha-MSH (1-13) (SEQ ID NO: 4) and alpha-MSH (11-13) (SEQ ID NO: 1) at concentrations of  $10^{-6}$  M significantly countered the growth enhancing effect of urokinase. Thus, alpha-MSH peptides can inhibit the growth of *Staphylococcus aureus*, an agent known to cause toxic shock



syndrome associated with tampon use, vaginitis, UTIs, urethritis, and balanoposthitis.

Please amend Paragraph 72 as follows:

At  $1 \times 10^6$ /ml in HBSS, these fungi were incubated in the presence or absence of alpha-MSH (1-13) (SEQ ID NO: 4), alpha-MSH (11-13) (SEQ ID NO: 1), or the CKPV (SEQ ID NO: 5) dimer at concentrations ranging from  $10^{-15}$  to  $10^{-4}$  M for two hours at  $37^\circ\text{C}$ . Cells were then washed in cold distilled water and diluted with HBSS to a concentration of 100 organisms/ml. One-milliliter aliquots were then dispensed on blood agar plates and incubated for 48 hours at  $37^\circ\text{C}$ . The organism's viability was estimated from the number of colonies formed.

Please amend Paragraph 73 as follows:

Figure 3 shows that alpha-MSH(1-13) (SEQ ID NO: 4), alpha-MSH(11-13) (SEQ ID NO: 1), and the CKPV (SEQ ID NO: 5) dimer greatly reduced the ability of *C. albicans* to form colonies at concentrations ranging from  $10^{-12}$  to  $10^{-4}$  M ( $p < 0.01$  vs. control). Thus, this demonstrates that alpha-MSH peptides can inhibit the growth of *Candida albicans*, an agent known to cause candidiasis, vaginitis, urethritis, and balanoposthitis.

Please amend Paragraph 75 as follows:

Alpha-MSH (1-13) (SEQ ID NO: 4), (4-10) (SEQ ID NO: 2), (6-13) (SEQ ID NO: 3), (11-13) (SEQ ID NO: 1), ACTH (1-39) (SEQ ID NO: 9), (18-39) (SEQ ID NO: 10), and fluconazole, at concentrations of  $10^{-6}$  to  $10^{-4}$  M, were tested against *C. albicans* using the same procedures as in Example II. Figure 4 shows that

compared with fluconazole, alpha-MSH (11-13) (SEQ ID NO: 1), (6-13) (SEQ ID NO: 3), and (1-13) (SEQ ID NO: 4) were most effective against *C. albicans*. Their inhibitory activities were similar to fluconazole at the same molar concentration. In contrast, the “core” alpha-MSH sequence (4-10) (SEQ ID NO: 2), which has behavioral effects but little anti-inflammatory activity, caused approximately 50% inhibition of colony forming units (CFU). Although this inhibitory effect was substantial ( $p < 0.01$  vs. control), it was significantly less potent than alpha-MSH fragments bearing the KPV signal sequence, i.e. alpha-MSH (6-13) (SEQ ID NO: 3) and (11-13) (SEQ ID NO: 1) ( $p < 0.01$ ), or the parent molecule alpha-MSH (1-13) (SEQ ID NO: 4) ( $p < 0.05$ ). Figure 4 also shows that ACTH (1-39) (SEQ ID NO: 12) (SEQ ID NO: 9) and the ACTH fragment (18-39) (SEQ ID NO: 13) (SEQ ID NO: 10) did not reduce *C. albicans* viability. Even at a higher concentration of  $10^{-4}$  M, which is not shown in the figures, ACTH peptides were likewise ineffective.

Please amend Paragraph 99 as follows:

To determine the level of NF- $\kappa$ B activity, nuclear extracts were prepared from  $20 \times 10^6$  U1 cells ( $2 \times 10^5$ /ml in complete medium) stimulated for four hours with TNF- $\alpha$  (20 ng/ml) in the presence or absence of  $10^{-5}$  M alpha-MSH (11-13) (SEQ ID NO: 1). Cells were washed once with cold PBS, and twice with buffer A (10 mM Hepes pH 7.9, 1.5 mM  $MgCl_2$ , 10 mM KCl, 0.5 mM PMSF and 0.5 mM DTT), centrifuged, and incubated for ten minutes on ice in buffer A plus 0.1% NP-40. Afterwards, the supernatants were removed, and the nuclear pellets were

resuspended in 15µl of buffer C (20 mM Hepes pH 7.9, 1.5 mM MgCl<sub>2</sub>, 0.42 M KCl, 0.2 mM EDTA, 25% glycerol, 0.5 mM PMSF, and 0.5 mM DTT), incubated for 15 minutes on ice, mixed, and then centrifuged. The supernatants were diluted with 75 µl of modified buffer D (20 mM Hepes, pH 7.9, 0.05 mM KCl, 0.2 mM EDTA, 20% glycerol, 0.5 mM PMSF, and 0.5 mM DTT) and stored at -80°C. The binding reaction was carried out for fifteen minutes at room temperature with 10µg of nuclear extract protein and 0.5 ng of <sup>32</sup>P-labeled NF-κB (30,000 cpm/µl) or AP1 consensus in buffer A (12 mM Tris-HCl pH 7.8, 60 mM KCl, 0.2 mM EDTA, 0.3 mM DTT), plus 10% glycerol, 2 µg/ml bovine serum albumin and 1 µg/ml single stranded DNA (Pharmacia Biotech). The oligonucleotides for NF-κB used in these studies were: + gat cca agg gga ctt tcc gct ggg gac ttt cca tg (SEQ ID NO: 14) (SEQ ID NO: 11), and – gat cca tgg aaa gtc ccc agc gga aag tcc cct tg (SEQ ID NO: 15) (SEQ ID NO: 12). Each oligonucleotide was annealed to its complementary strand and end-labeled with <sup>32</sup>P-γ-ATP using polynucleotide kinase. For the determination of specific bands, nuclear extracts were first incubated with 100 fold excess unlabeled probe for five minutes, before incubation with a labeled probe. The mixtures were then run on 5% (30:1) acrylamide gel in 1x TBE. The gels were dried and autoradiographed. Please replace Paragraph 109 as follows:

~~Although specific amino acid sequences described here are effective, it is clear to those familiar with the art that amino acids can be substituted or deleted without altering the effectiveness of the peptides. Further, it is known that~~

stabilization of the alpha-MSH sequence can greatly increase the activity of the peptide and that substitution of D-amino acid forms for L-forms can improve or decrease the effectiveness of the peptides. For example, a stable analog of alpha-MSH, [Nle<sup>4</sup>,D-Phe<sup>7</sup>]-alpha-MSH, which is known to have marked biological activity on melanocytes and melanoma cells, is approximately ten times more potent than the parent peptide in reducing fever. Further, adding amino acids to the C-terminal of alpha-MSH (11-13) (SEQ ID NO: 1) sequence can reduce or enhance antipyretic potency. Addition of glycine to form the 10-13 sequence (SEQ ID NO: 5) slightly decreased potency; the 9-13 sequence (SEQ ID NO: 6) was almost devoid of activity, whereas the potency of the 8-13 sequence (SEQ ID NO: 7) was greater than that of the 11-13 sequence (SEQ ID NO: 1). It is known that Ac-[D-K<sub>11</sub>]-alpha-MSH 11-13-NH<sub>2</sub> has the same general potency as the L-form of the tripeptide alpha-MSH (11-13) (SEQ ID NO: 1). Certain references, however, have shown substitution with D-proline in position 12 of the tripeptide rendered it inactive. See e.g., Holdeman, M., et. al., Antipyretic Activity of a Potent alpha-MSH Analog, *Peptides* 6, 273-5 (1985). Deeter, L. B., et. al., Antipyretic Properties of Centrally Administered alpha-MSH Fragments in the Rabbit, *Peptides* 9, 1285-8 (1989). Hiltz, M. E., Anti-inflammatory Activity of alpha-MSH (11-13) Analogs: Influences of Alterations in Stereochemistry, *Peptides* 12, 767-71 (1991).

Although specific amino acid sequences described here are effective, it is clear to those familiar with the art that amino acids can be substituted or deleted

without altering the effectiveness of the peptides. Further, it is known that stabilization of the alpha-MSH sequence can greatly increase the activity of the peptide and that substitution of D-amino acid forms for L-forms can improve or decrease the effectiveness of the peptides. For example, a stable analog of alpha-MSH, [Nle<sup>4</sup>,D-Phe<sup>7</sup>]-alpha-MSH, which is known to have marked biological activity on melanocytes and melanoma cells, is approximately ten times more potent than the parent peptide in reducing fever. Further, adding amino acids to the C-terminal of alpha-MSH (11-13) (SEQ ID NO: 1) sequence can reduce or enhance antipyretic potency. Addition of glycine to form the 10-13 sequence (SEQ ID NO: 13) slightly decreased potency; the 9-13 sequence (SEQ ID NO: 14) was almost devoid of activity, whereas the potency of the 8-13 sequence (SEQ ID NO: 15) was greater than that of the 11-13 sequence (SEQ ID NO: 1). It is known that Ac-[D-K<sub>11</sub>]-alpha-MSH 11-13-NH<sub>2</sub> has the same general potency as the L-form of the tripeptide alpha-MSH (11-13) (SEQ ID NO: 1). Certain references, however, have shown substitution with D-proline in position 12 of the tripeptide rendered it inactive. See e.g., Holdeman, M., et. al., Antipyretic Activity of a Potent alpha-MSH Analog, *Peptides* 6, 273-5 (1985). Deeter, L. B., et. al., Antipyretic Properties of Centrally Administered alpha-MSH Fragments in the Rabbit, *Peptides* 9, 1285-8 (1989). Hiltz, M. E., Anti-inflammatory Activity of alpha-MSH (11-13) Analogs: Influences of Alterations in Stereochemistry, *Peptides* 12, 767-71 (1991).

Please replace Paragraph 113 as follows:

Results illustrated in Figures 17-19 and show the resulting CFUs under the conditions described above for the particular fungus identified. The figures include the resulting CFUs in the presence of no alpha-MSH peptides (designated as "0" in Figures 17-19),  $10^{-4}$  M of KPV [designated as "-4" in Figures 17-19],  $10^{-7}$  M of the CKPV (SEQ ID NO: 5) dimer [designated as "-7" in Figures 17-19],  $10^{-6}$  M of the CKPV (SEQ ID NO: 5) dimer [designated as "-6" in Figures 1-3],  $10^{-5}$  M of the CKPV (SEQ ID NO: 5) dimer [designated as "-5" in Figures 17-19], and  $10^{-4}$  M of the CKPV (SEQ ID NO: 5) dimer [designated as "-4" in Figures 17-19]. Figure 17 shows that at the same molarity, the CKPV (SEQ ID NO: 5) dimer is more than twice as effective as the KPV monomer in treating *C. albicans*. Figure 18 shows that at the same molarity, the CKPV (SEQ ID NO: 5) dimer is more than twice as effective as the KPV monomer in treating *C. krusei*. Figure 19 shows that at the same molarity the CKPV (SEQ ID NO: 5) dimer is more than twice as effective as the KPV monomer in treating *C. glabrata*.

Results illustrated in Figures 17-19 and show the resulting CFUs under the conditions described above for the particular fungus identified. The figures include the resulting CFUs in the presence of no alpha-MSH peptides (designated as "0" in Figures 17-19),  $10^{-4}$  M of KPV [designated as "-4" in Figures 17-19],  $10^{-7}$  M of the CKPV (SEQ ID NO: 5) dimer [designated as "-7" in Figures 17-19],  $10^{-6}$  M of the CKPV dimer [designated as "-6" in Figures 1-3],  $10^{-5}$  M of the CKPV (SEQ ID NO: 5) dimer [designated as "-5" in Figures 17-19], and  $10^{-4}$  M

of the CKPV (SEQ ID NO: 5) dimer [designated as "-4" in Figures 17-19]. Figure 17 shows that at the same molarity, the CKPV (SEQ ID NO: 5) dimer is more than twice as effective as the KPV monomer in treating *C. albicans*. Figure 18 shows that at the same molarity, the CKPV (SEQ ID NO: 5) dimer is more than twice as effective as the KPV monomer in treating *C. krusei*. Figure 19 shows that at the same molarity the CKPV (SEQ ID NO: 5) dimer is more than twice as effective as the KPV monomer in treating *C. glabrata*.